

**REMARKS**

**I     Amendment to the Specification**

The specification is amended by adding the sentence, “This application is the United States national stage application under 35 U.S.C. § 371 of the International Patent Cooperation Treaty application PCT/FR98/02899, filed December 29, 1998, which claims priority to Application No.: FR 97 16,673, filed December 30, 1997.” No new matter has been added.

**II    Status of the Claims**

In claim 6, the first element is amended with the addition of the word “contacting” and the deletion of the words “bringing” and “into contact.” Additionally, the third element is added by the phrase “removing the rest of said biological sample after said antigen/antibody complex is formed; and.” This is supported by the specification (*see* from page 12, line 37 through page 13, line 20). Claim 6 is also amended to add a whereby clause that correlates the final step with the preamble of the claim. Claim 8 is amended by adding the “Ser-Cit-His” description of the tripeptide motif, and deleting the phrase “specifically present” and the reference to the non-elected subject matter in “SEQ ID NO: 5 or SEQ ID NO: 6.” New claims 13-15 have been added by this amendment. The support for the new claims can be found on page 5 line 38 through page 6, line 6 of the specification. No new matter is added by this amendment.

### **III     Priority**

The Examiner suggests that the first sentence of the specification must contain a specific reference to prior applications if benefits are to be claimed according to 37 C.F.R. § 1.78.

Applicants argue that this application is a national stage application under 35 U.S.C. § 371. No priority claim under 35 U.S.C. § 120 is being made. Therefore, no reference to the PCT in the first line of the specification is required. Nevertheless, Applicants amended the specification with a sentence to cross reference to the International application PCT/FR98/02899.

### **IV     Information Disclosure Statement**

In this Office Action, the Examiner requests an English translation of WO 98 08946. According to MPEP § 609, “the requirement for a concise explanation of relevance can be satisfied by submitting an English-language version of the search report or action which indicate the degree of relevance found by the foreign office.” Applicants would bring to the attention of the Examiner that the submission of the IDS on June 30, 2000 included the explanation and the English translation of the search report. For the convenience of the Examiner, copies of the IDS and the English translation of the search report are included with this filing. In addition, as noted in the IDS filed June 30, 2000, Applicants stated that “An international Search Report, citing the documents and setting forth the relevance thereof are also enclosed for the Examiner’s consideration. In addition to this citation the relevance of French language document WO 98/08946 is noted on page 4, lines 21-32, of the specification, which cites the French priority document of this publication.”

**V     Use of Trademarks in the Specification**

The Examiner requested that all trademarks are to be capitalized and accompanied with generic terminology. The trademarks and tradenames in the specification are all correctly indicative of their status to the best of Applicants' knowledge. One of skill in the art would be very familiar with these materials. Applicants are not aware of any requirement to provide "generic terminology." No trademarks or tradenames are used in the claims. The Office Action does not set forth reasons why added text to supply generic terminology would be required

**VI     Rejection Under 35 U.S.C. § 112**

**(a) 35 U.S.C. § 112, First Paragraph**

Claim 6 is rejected under 35 U.S.C. § 112, first paragraph, for being based a disclosure which is not enabling because the method has insufficient steps. According to the Examiner, the recited claim does not include the steps of "contact, detection and correlation." Also, claim 8 is rejected under 35 U.S.C. § 112, first paragraph, for containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention. According to the Examiner, the written description is not commensurate in scope with a peptide molecule comprising particular tripeptide motif's centered on a citrulline residue of SEQ ID NO:3, 5, and 6 as recited in claim 8. According to the Examiner, the language of claim 8 suggests that any amino acid can be present on either side of the citrulline, and such variants are not described in the specification.

Discussion

By this amendment, claim 6 is amended with the addition of the “contacting” and the “removing” and the equivalent of “detecting” steps and therefore the method is complete and enabling. Claim 8 is amended by adding “Ser-Cit-His” as the description of the tripeptide motif, and by deleting the non-elected subject matter in the SEQ ID NO: 5 and 6. As a result, the invention recited in the amended claim 8 is fully described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Applicants, at the time of the application was filed, had possession of the claimed invention. Therefore Applicants request that the rejection of claims 6 and 8 under 35 U.S.C. § 112, first paragraph, be withdrawn.

(b) 35 U.S.C. § 112, Second Paragraph

Claims 1, 3, and 5-12 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter. The Examiner requested that the meaning of the expression “tripeptide unit” in claim 1 be explained, and the “ambiguity” due to the phrase “specifically present” in claim 8 be removed. Also, claim 6 is rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential step that recites the “washing or removal of unbound materials” and the step that “identify reagent and sample contact” related “to the diagnosing and distinguishing of strokes.”

Discussion

The tripeptide motif Ser-Cit-His in claim 1 and in the amended claim 8 refers to the sequence of the three amino acids serine, citrulline and histidine being connected together by the

amide linkage between amino acid residues of proteins. This motif is recited as part of “an epitope recognized by antifilaggrin autoantibodies present in serum from rheumatoid arthritis patents” (*see* page 5, lines 21-23). Furthermore, the tripeptide motif can exist as part of larger peptides that are derived by citrullination of peptides such as a pentapeptide motif X1-Ser-Arg-His-X2 (*see* page 6, lines 1-2), a hexapeptide motif X0-X1-Ser-Arg-His-X2 (*see* page 6, lines 3-4) or a heptapeptide motif X0-X1-Ser-Arg-His-X2-X3 (*see* page 6, lines 4-5). Therefore, claims 1,3, 5-12 do not fail to particularly point out and distinctly claim the subject matter of the invention.

Furthermore, claims 6 is amended by the addition of the step that recites the removing and washing of unbound material. The Examiner’s referral to “detection of stroke” is not understood. Also, claim 8 is amended by deleting the phrase “specifically present” and therefore, the ambiguity derived from the phrase is removed. Therefore, Applicants respectfully request that the rejection of claims 1, 3, 5-12 under 35 U.S.C. § 112, second paragraph, be withdrawn.

## **XII Rejection Under 35 U.S.C. § 102**

Claims 1, 3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Biomerieux et. al (FR 96/10651), filed August 30, 1996. According to the Examiner, Applicants’ specification on page 4 (see lines 24-38) discloses the inventive concept in the French application FR 96/10651. It is not clear to the Examiner how the instant peptides differ from the ones taught by Biomerieux.

The prior art reference FR 96/10651 was filed on August 30, 1996 and published on March 6, 1998. In comparison, under 35 U.S.C. § 371, this application is a national stage

application of the application PCT/FR98/02899, filed December 29, 1998. Because the date of the reference, March 6, 1998, is less than one year before the effective filing date, December 29, 1998, of this application, the reference is not a proper reference under 35 U.S.C. § 102(b). Therefore, Applicants respectfully request that the rejection of claims 1, 3 and 5 under 35 U.S.C. 102(b) as being anticipated by Biomerieux be withdrawn.

In addition, Applicants note that the inventive entity herein is identical to the Biomerieux reference that has been cited as prior art. Thus, the reference is not available as prior art against this application, since no "other" person is involved.

### **XIII Rejection Under 35 U.S.C. § 103**

Claims 6, 7, 9-11 and 12 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Serre *et al.* (U.S. Patent No. 5,888,833) (*Serre*) in view of Biomerieux *et. al.* (FR 96/10651) (*Biomerieux*) filed August 30, 1996. According to the Examiner, *Serre* teaches methods and kits to diagnose rheumatoid arthritis (RA) via the contacting an antigen to a biological sample to form an immune complex with autoantibodies as an indicator of RA. However, the Examiner acknowledges that *Serre* differs from the claimed invention in that *Serre* does not specifically teach the peptide compositions or polypeptides derived from the sequence of filaggrin. However, according to the Examiner, *Biomerieux* teaches these compositions. The Examiner maintains that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to take the peptide compositions taught by *Biomerieux* and format them into an assay and kit to measure RA as in *Serre* because *Biomerieux* teaches that the replacement of Arg by Cit was essential in antigen-specific recognition by the autoantibodies.

For the reasons outlined above, *Biomerieux* is not available as prior art to this application.  
Thus Applicants respectfully request withdrawal of this rejection.

**IX     Conclusion**

In view of the foregoing, Applicants respectfully request withdrawal of the restriction requirement and continuation of prosecution.

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R § 1.16 and § 1.17 which may be required, or credit any overpayment to Deposit Account No. 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully submitted,

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**Version of Amended Claims with Markings to Show Changes Made**

**IN THE SPECIFICATION:**

1. On page 1, at line 3, before the paragraph starting with, "The present invention relates ..., " please insert the following paragraph:

--This application is the United States national stage application under 35 U.S.C. § 371 of the International application PCT/FR98/02899, filed December 29, 1998, which claims priority to Application No.: FR 97 16,673, filed December 30, 1997.--

**IN THE CLAIMS:**

6. (Amended) A method for detecting rheumatoid arthritis-specific autoantibodies in a biological sample [~~method~~] comprising:

[~~bringing~~] contacting said biological sample [~~into contact~~] <sup>at</sup> with least one antigen

according to Claim 1 under conditions which allow the formation of an antigen/antibody complex with any rheumatoid arthritis-specific autoantibodies possibly present in the biological sample;

removing (the rest) of <sup>unbound complex</sup> said biological sample after said antigen/antibody complex is formed; and

detecting, by any suitable means, any antigen/antibody complex formed, whereby the presence or absence of rheumatoid arthritis-specific autoantibodies in said biological sample is determined.

8. (Amended) The artificial antigen of Claim 3 wherein the antigen consists of at least one peptide comprising a tripeptide motif Ser-Cit-His, in which Cit represents a citrulline residue, ~~[centered on a citrulline residue,]~~ which is ~~[specifically present]~~ on at least one of the citrullinated peptides derived from the ~~[sequences]~~ sequence SEQ ID NO: 3~~[, SEQ ID NO: 5 or SEQ ID NO: 6].~~

*conciled*

New claims 13-15 are added in this amendment.